Clinical Policy Bulletin: Bio-Surgery: Medicinal Leech Therapy and Medical Maggots

Policy History

Last Review : 09/03/2010
Effective: 08/17/2001
Next Review : 07/14/2011
Review History
Definitions

Additional Information

Clinical Policy Bulletin Notes

Number: 0556

Policy

I. Aetna considers medicinal leech (Hirudo medicinalis) therapy medically necessary for any of the following conditions:

   A. Poor venous drainage (venous congestion/venous outflow obstruction); *or*
   B. Salvage of vascularly compromised flaps (muscle, skin, and fat tissue surgically removed from one part of body to another); *or*
   C. Salvage of vascularly compromised replants (limbs or other body parts re-attached after traumatic amputation).

II. Aetna considers medicinal leech therapy experimental and investigational for treating cancer pain, knee osteoarthritis, inadequate arterial supply or tissue ischemia, and for all other indications.

III. Aetna considers medical maggots medically necessary for the debridement of *any* of the following non-healing necrotic skin and soft tissue wounds:

   A. Neuropathic foot ulcers; *or*
   B. Non-healing traumatic or post surgical-wounds; *or*
   C. Pressure ulcers; *or*
   D. Venous stasis ulcers.

Background

The medicinal leech, *Hirudo medicinalis*, has been used increasingly for relief of venous congestion, especially for salvage of compromised pedicled flaps and microvascular free-tissue transfer, digital re-implantation, and breast reconstruction. Leech therapy for compromised flaps is best used early since flaps demonstrate

significantly decreased survival after 3 hours if venous congestion is not relieved. If venous pooling occurs around a flap or replant, the skin becomes cyanotic, cool, and hard. If capillary refill time (CRT) remains more than 3 seconds the flap or replant will not survive. The objective of leech therapy is for the affected area to become pink and warm, with a CRT of less than 2 seconds.

When leeches begin feeding, they inject salivary components (e.g., hirudin) that inhibit both platelet aggregation and the coagulation cascade. This results in a marked relief of venous congestion. The anti-coagulant causes the bite to ooze for up to 48 hours following detachment, further relieving venous congestion. By feeding for 10 to 60 minutes, leeches consume from 1 to 2 teaspoons of blood. Results from clinical studies showed that the success rate of salvaging tissue with medicinal leech therapy is 70 to 80%. On June 28, 2004, the Food and Drug Administration (FDA) had for the first time cleared the commercial marketing of leeches for medicinal purposes (in skin grafts and reattachment surgery).

Recently, leech therapy has also been suggested to be an effective treatment for rapid reduction of pain associated with osteoarthritis of the knee (Michalsen, et al., 2002). However, its effectiveness in treating osteoarthritis (OA) of the knee needs to be validated in larger randomized controlled studies. In a follow-up randomized controlled study, Michalsen, et al. (2003) evaluated the effectiveness of leech therapy for symptomatic relief of patients with OA of the knee (n = 51). Patients received a single treatment with 4 to 6 locally applied leeches (leech therapy group) or a 28-day topical diclofenac regimen (control group). The primary end point, pain at day 7, was reduced from a mean (+/-SD) of 53.5 +/- 13.7 to 19.3 +/- 12.2 after leech therapy compared with 51.5 +/- 16.8 to 42.4 +/- 19.7 with topical diclofenac. Although the difference between group pain scores was no longer significant after day 7, differences for function, stiffness, and total symptoms remained significant in favor of leech therapy until the end of study and for quality of life until day 28. The authors concluded that leech therapy helps relieve symptoms in patients with OA of the knee. The potential of leech therapy for treating OA and the pharmacological properties of leech saliva remain to be clarified.

In an editorial that accompanied the article by Michalsen, et al., Hochberg (2003) discussed some of the drawbacks of this paper. A lack of blinding of the patients as well as the researchers is a major pitfall because it raises concerns regarding measurement bias, especially since the outcome measures were all subjective. Also, 7 days is a short time frame for measuring the primary outcome measure since OA is a chronic condition. Furthermore, patients in both groups seldom used rescue therapy, suggesting that, despite the observed significant differences in pain scores at day 7, both groups may have been satisfied with their responses to study interventions. Thus, it is still unclear whether leech therapy is effective in treating knee pain in patients with OA.

Kalender and colleagues (2010) reported a case of severe pain related to advanced stage cancer successfully treated by self-applied leeches. A 62-year-old male patient with synchronous renal cell carcinoma and leiomyosarcoma was admitted with severe pain in the lumbar region. The pain was refractory to radiotherapy, and systemic and epidural analgesic infusion. Two months the patient came to the clinic in good condition free of pain. The patient reported outpatient self-treatment with seven leeches to the lumbar region in the interim that resulted in complete healing of pain. The authors concluded that this is the first report indicating possible activity of

leeches in cancer pain. The finding of this case report needs to be validated by well-designed studies.;

Medicinal leech therapy is usually carried out for 4 to 5 days for patients with replant; it may be performed for 6 to 10 days for patients with compromised flaps.

A complication of leech therapy is the risk of infection; thus, it is recommended that therapy not be used in the presence of non-viable tissue.

Patients with HIV infection, or individuals taking immunosuppressive medications should not undergo leech therapy because of the risk of overwhelming bacterial sepsis.

During the 1930s, maggot debridement therapy (MDT) was used routinely for treating bone and soft-tissue infections. Its use was supplanted by the introduction of new antibiotics and improvements in wound care. Recently, however, there has been a resurgence in the use of maggot therapy.

Medical maggots are blow fly (i.e., *phaenicia sericata)* larvae. Medical maggots, or larval therapy, is also known as maggot therapy, maggot dressings, green blow fly maggots, bio-surgery, disinfected maggots, sterile maggots, therapeutic maggots, debriding maggots, maggot debridement therapy, or MDT dressings. Medical maggots secret digestive enzymes that selectively dissolve necrotic tissue, disinfect the wound, and stimulate wound healing.

Medical maggots received 510(k) marketing clearance by the U.S. Food and Drug Administration (FDA) and are intended to debride non-healing necrotic skin and soft tissue wounds, including pressure ulcers, venous stasis ulcers, neuropathic foot ulcers, and non-healing traumatic or post surgical wounds. According to information submitted by the manufacturer to the FDA, the fly eggs are chemically disinfected before being placed in sterile vials for transport. The dressings used to confine them on the wound are called "Creature Comforts" and are designed to create a confining "cage dressing." They are applied directly to the wound surface in a dose of 5-8 maggots per square cm. The dressings are left in place on the wound for a "cycle" of 48 hours (24-72 hours). One to 3 cycles are applied weekly. Most wounds require 2-6 cycles for complete debridement.

In a prospective study, Sherman, et al. (1995) evaluated the utility of maggot therapy (MT) for treating pressure ulcers in spinal cord injury patients. Eight patients received MT after a baseline assessment of healing under conventional therapy (defined as any therapy prescribed by the patient's primary care team). Surface area, tissue quality and healing rates were monitored weekly. Maggot therapy debrided most of the necrotic wounds within 1 week, which was more rapid than all other non-surgical methods. Wound healing was more rapid during MT than during antecedent conventional therapy ($p = 0.01$). No complications were noted.

In an abstract presented during the European Association for the Study of Diabetes Annual Meeting (2000), Markevich, et al. reported the results of a 30-month randomized, multi-center, double-blind controlled clinical trial of MT for diabetic neuropathic foot wounds as compared with conventional modern treatment in 140 diabetic patients. Sterile maggots (larvae) of the green-bottle fly (Lucilia sericata) were applied to the wound (6-10 per square cm) for 72 hours. At 10 days, granulation tissue covered greater than 50% of the wound in the MT group versus 34% in the

control, and the wound area had decreased by greater than 50% in the MT group versus 27% in the control. This may be a useful method for debridement of necrotic tissue from diabetic foot wounds with particular benefits in stimulating tissue growth and improving the rate of healing (Bloomgarden, 2001).

Wayman, et al. (2000) examined the clinical efficacy and cost effectiveness of larval therapy in the debridement of sloughy venous ulcers . Twelve patients with sloughy venous ulcers were randomized to receive either larval debridement therapy (LDT) or a hydrogel (the control). Effective debridement occurred with a maximum of 1 larval application in 6/6 patients; 4/6 patients in the hydrogel group still required dressings at one month. The median cost of treatment of the larval group was 78.64 pounds compared with 136.23 pounds for the control treatment group ($p < 0.05$).

Sherman (2002) compared MT versus conservative debridement therapy for the treatment of pressure ulcers in 103 in-patients with 145 pressure ulcers. Sixty-one ulcers in 50 patients received MT at some point during their monitored course and 84 ulcers in 70 patients did not. Debridement and wound healing could be quantified for 43 maggot-treated wounds and 49 conventionally treated wounds. Eighty percent of maggot-treated wounds were completely debrided, while only 48% of wounds were completely debrided with conventional therapy alone ($p = 0.021$). Within 3 weeks, maggot-treated wounds contained one-third the necrotic tissue ($p = 0.05$) and twice the granulation tissue ($p < 0.001$), compared to non-maggot-treated wounds. Of the 31 measurable maggot-treated wounds monitored initially during conventional therapy, necrotic tissue decreased 0.2 square cm per week during conventional therapy, while total wound area increased 1.2 square cm per week. During maggot therapy, necrotic tissue decreased 0.8 cm2 per week ($p = 0.003$) and total wound surface area decreased 1.2 cm2 per week ($p = 0.001$). The author concluded that MT was more effective and efficient in debriding chronic pressure ulcers than the conventional treatments prescribed, patients readily accepted MT and adverse events were uncommon.

Sherman (2003) retrospectively assessed the efficacy of MT for treating foot and leg ulcers in 18 diabetic patients who failed conventional therapy. Of the 20 non-healing ulcers, 6 wounds were treated with conventional therapy, 6 with MT, and 8 with conventional therapy first, then MT. Repeated measures ANOVA indicated no significant change in necrotic tissue, except when factoring for treatment ($F [1.7, 34] = 5.27$, $p = 0.013$). During the first 14 days of conventional therapy, there was no significant debridement of necrotic tissue; during the same period with MT, necrotic tissue decreased by an average of 4.1 square cm ($p = 0.02$). After 5 weeks of therapy, conventionally treated wounds were still covered with necrotic tissue over 33% of their surface, whereas after only 4 weeks of therapy maggot-treated wounds were completely debrided ($p = 0.001$). Maggot therapy was also associated with hastened growth of granulation tissue and greater wound healing rates.

Sherman and Shimoda (2004) evaluated post-operative complications of pre-surgical wounds treated with MDT versus a matched group of patients who were not treated with MDT. Ten wounds were debrided by maggots within 1-17 days prior to surgical closure. Debridement was effective in all cases, and there were no post-operative wound infections. Six (32%) of 19 wounds not treated pre-surgically with MDT developed post-operative wound infections (95% CI, 10%-54%; $p < 0.05$). Pre-surgical MDT was effective in preparing the wound bed for surgical closure, without increased risk of post-surgical wound infection.

Armstrong, et al. (2005) assessed MDT in 60 non-ambulatory patients (mean age 72.2 years) with neuro-ischemic diabetic foot wounds and peripheral vascular disease. Twenty-seven of these patients (45%) healed during 6 months of review. There was no significant difference in the proportion of patients healing in the MDT versus control group (57% versus 33%). Of patients who healed, time to healing was significantly shorter in the MT than in the control group (18.5 +/- 4.8 versus 22.4 +/- 4.4 weeks). Approximately 1 in 5 patients (22%) underwent a high-level (above-the-foot) amputation. Patients in the control group were 3 times as likely to undergo amputation (33% versus 10%). Although there was no significant difference in infection prevalence in patients undergoing MT versus controls (80% versus 60%), there were significantly more antibiotic-free days during follow-up in patients who received MT (126.8 +/- 30.3 versus 81.9 +/- 42.1 days). Maggot debridement therapy reduced short-term morbidity in non-ambulatory patients with diabetic foot wounds.

Tantawi, et al. (2007) assessed the clinical and microbiological efficacy of MDT in the management of diabetic foot ulcers unresponsive to conventional treatment and surgical intervention. Consecutive diabetic patients with foot wounds were selected for MDT. Lucilia sericata medicinal maggots were applied to the ulcers for 3 days per week. Changes in the percentage of necrotic tissue and ulcer surface area were recorded each week over the 12-week follow-up period. Semi-quantitative swab technique was used to determine the bacterial load before and after MDT. The sample comprised 10 patients with 13 diabetic foot ulcers. The mean baseline ulcer surface area was 23.5 square cm (range 1.3-63.1) and the mean percentage of necrotic tissue was 74.9% (range 29.9-100). Complete debridement was achieved in all ulcers in a mean of 1.9 weeks (range 1-4). Five ulcers (38.5%) were completely debrided with one 3-day MDT cycle. The mean reduction in ulcer size was significant at 90.2% and this occurred in a mean of 8.1 weeks (range 2-12). The mean weekly reduction in ulcer size was 16.1% (range 8.3-50). Full wound healing occurred in 11 ulcers (84.6%) within a mean of 7.3 weeks (range 2-10). The bacterial load of all ulcers reduced sharply after the first MDT cycle to below the 10^5 threshold, which facilitates healing. The authors concluded that the results highlight the potential benefits of MDT in diabetic wound care in developing countries and that MDT proved to be a rapid, simple and efficient method of treating these ulcers.

A review of MDT in chronic wound care by Chan, et al. (2007) stated that MDT has been shown to be a safe and effective means of chronic wound management, however, there are a number of limitations when considering its local applicability. Future development of the delivery system may help to overcome some of these limitations and improve its acceptability.

The VenUS II trial, a multi-center prospective clinical study compared the clinical and cost effectiveness of 2 types of larval therapy (loose and bagged) with a standard debridement intervention (hydrogel). Patients (n = 267) with at least one venous or mixed venous and arterial ulcer with at least 25% coverage of slough or necrotic tissue, and an ankle brachial pressure index of 0.6 or more were enrolled in the study. The primary outcome was time to healing of the largest eligible ulcer. Secondary outcomes were time to debridement, health related quality of life (SF-12), bacterial load, presence of methicillin resistant Staphylococcus aureus (MRSA), adverse events, and ulcer related pain (visual analogue scale, from 0 mm for no pain to 150 mm for worst pain imaginable). The authors reported that time to healing was not significantly different between the loose or bagged larvae group and the hydrogel group

(hazard ratio for healing using larvae versus hydrogel 1.13, 95% confidence interval 0.76 to 1.68; p = 0.54). Larval therapy significantly reduced the time to debridement (2.31, 1.65 to 3.2; p < 0.001). Health related quality of life and change in bacterial load over time were not significantly different between the groups. Seven percent of participants had MRSA at baseline and there was no difference found between larval therapy and hydrogel in their ability to eradicate MRSA by the end of the debridement phase (75% (9/12) versus 50% (3/6); p = 0.34), although this comparison was underpowered. Mean ulcer related pain scores were higher in either larvae group compared with hydrogel (mean difference in pain score: loose larvae versus hydrogel 46.74 (95% confidence interval 32.44 to 61.04), p < 0.001; bagged larvae versus hydrogel 38.58 (23.46 to 53.70), p < 0.001). The authors concluded that larval therapy did not improve the rate of healing of sloughy or necrotic leg ulcers or reduce bacterial load compared with hydrogel and was associated with significantly more ulcer related pain but it did significantly reduce the time to debridement compared with hydrogel (Dumville, et al., 2009).

To assess the cost effectiveness of larval therapy compared with hydrogel in the management of leg ulcers, Soares and colleagues (2009) carried out a cost effectiveness and cost utility analyses alongside the VenUS II trial. The time horizon was 12 months and costs were estimated from the United Kingdom National Health Service perspective. Cost effectiveness outcomes were expressed in terms of incremental costs per ulcer-free day (cost effectiveness analysis) and incremental costs per quality adjusted life years (cost utility analysis). The larvae arms were pooled for the main analysis. Treatment with larval therapy cost, on average, pound 96.70 (euro 109.61; $140.57) more per participant per year (95% confidence interval -pound 491.9 to pound 685.8) than treatment with hydrogel. Participants treated with larval therapy healed, on average, 2.42 days before those in the hydrogel arm (95% confidence interval -0.95 to 31.91 days) and had a slightly better health related quality of life, as the annual difference in QALYs was 0.011 (95% confidence interval -0.067 to 0.071). However, none of these differences was statistically significant. The incremental cost effectiveness ratio for the base case analysis was estimated at pound 8826 per QALY gained and pound 40 per ulcer-free day. Considerable uncertainty surrounds the outcome estimates. The authors concluded that debridement of sloughy or necrotic leg ulcers with larval therapy is likely to produce similar health benefits and have similar costs to treatment with hydrogel.

CPT Codes / HCPCS Codes / ICD-9 Codes

Medicinal leech therapy:

There is no specific CPT code for medicinal leech therapy:

ICD-9 codes covered if selection criteria are met:

459.2	Compression of vein
459.81, 459.89	Venous (peripheral) insufficiency, unspecified, and other specified disorders of circulatory system
996.52	Mechanical complications due to graft of other tissue, not elsewhere classified

996.90 - 996.96	Complications of reattached extremity or body part
V49.60 - V49.77	Upper and lower limb amputation status

ICD-9 codes not covered for indications listed in the CPB:

042	Human immunodeficiency virus [HIV] disease
279.00 - 279.9	Disorders involving the immune mechanism
338.3	Neoplasm related pain (acute) (chronic)
715.16, 715.26, 715.36, 715.96	Osteoarthrosis of knee, localized, primary or secondary, not specified whether primary or secondary, or unspecified whether generalized or localized
V08	Asymptomatic human immunodeficiency virus [HIV] infection status

Medical maggots:

CPT codes covered if selection criteria are met:

97602

ICD-9 codes covered if selection criteria are met:

249.80 - 249.81	Secondary diabetes mellitus with other specified manifestations
250.80 - 250.83	Diabetes with other specified manifestations
454.0	Varicose veins of lower extremities with ulcer
454.2	Varicose veins of lower extremities with ulcer and inflammation
707.00 - 707.9	Chronic ulcer of skin
872.10 - 897.7	Open wounds, complicated [non-healing]
998.83	Non-healing surgical wound

The above policy is based on the following references:

Medicinal Leech Therapy

1. Voge C, Lehnherr SM. Leeches. Nursing. 1999;29(11):46-47.
2. Utley DS, Koch RJ, Goode RL. The failing flap in facial plastic and reconstructive surgery: Role of the medicinal leech. Laryngoscope. 1998;108(8 Pt 1):1129-1135.
3. de Chalain TM. Exploring the use of the medicinal leech: A clinical risk-benefit analysis. J Reconstr Microsurg. 1996;12(3):165-172.

4. Haycox C, Odland PB, Coltrera MD, Raugi GJ. Indications and complications of medicinal leech therapy. J Am Acad Dermatol. 1995;33(6):1053-1055.
5. Michalsen A, Moebus S, Spahn G, et al. Leech therapy for symptomatic treatment of knee osteoarthritis: Results and implications of a pilot study. Altern Ther Health Med. 2002;8(5):84-88.
6. Michalsen A, Klotz S, Ludtke R, et al. Effectiveness of leech therapy in osteoarthritis of the knee: A randomized, controlled trial. Ann Intern Med. 2003;139(9):724-730.
7. Hochberg MC. Multidisciplinary integrative approach to treating knee pain in patients with osteoarthritis. Ann Intern Med. 2003;139(9):781-783.
8. U.S. Food and Drug Administration (FDA). FDA clears medicinal leeches for marketing. FDA Talk Paper. T04-19. Rockville, MD: FDA; June 28, 2004. Available at: http://www.fda.gov/bbs/topics/answers/2004/ANS01294.html. Accessed June 30, 2004.
9. Frodel JL Jr, Barth P, Wagner J. Salvage of partial facial soft tissue avulsions with medicinal leeches. Otolaryngol Head Neck Surg. 2004;131(6):934-939.
10. Whitaker IS, Cheung CK, Chahal CA, et al. By what mechanism do leeches help to salvage ischaemic tissues? A review. Br J Oral Maxillofac Surg. 2005;43(2):155-160.
11. Durrant C, Townley WA, Ramkumar S, Khoo CT. Forgotten digital tourniquet: Salvage of an ischaemic finger by application of medicinal leeches. Ann R Coll Surg Engl. 2006;88(5):462-464.
12. Knobloch K, Gohritz A, Busch K, et al. Hirudo medicinalis-leech applications in plastic and reconstructive microsurgery -- a literature review. Handchir Mikrochir Plast Chir. 2007;39(2):103-107.
13. Kalender ME, Comez G, Sevinc A, et al. Leech therapy for symptomatic relief of cancer pain. Pain Med. 2010;11(3):443-445.

Medical Maggots

1. Bradley M, Cullum N, Sheldon T. The debridement of chronic wounds: A systematic review. Health Technol Assess. 1999;3(17 Pt 1). Available at: http://www.ncchta.org/fullmono/mon3171.pdf. Accessed March 5, 2009.
2. J Smith. Debridement of diabetic foot ulcers. Cochrane Database of Systematic Reviews. 2002, Issue 4. Art. No.: CD003556.
3. Bloomgarden ZT. European Association for the Study of Diabetes Annual Meeting, 2000: Pathogenesis of type 2 diabetes, vascular disease, and neuropathy. Diabetes Care. 2001;24(6):1115-1119.
4. Wayman J, Nirojogi V, Walker A, et al. The cost effectiveness of larval therapy in venous ulcers. J Tissue Viability. 2000;10(3):91-94.
5. Sherman RA, Shimoda KJ. Presurgical maggot debridement of soft tissue wounds is associated with decreased rates of postoperative infection. Clin Infect Dis. 2004 Oct 1;39(7):1067-70. Epub 2004 Sep 1.
6. Stoddard SR, Sherman RA, Mason BE, et al. Maggot debridement therapy. An alternative treatment for nonhealing ulcers. J Am Podiatr Med Assoc. 1995;85(4):218-321.
7. Sherman RA, Wyle F, Vulpe M. Maggot therapy for treating pressure ulcers in spinal cord injury patients. J Spinal Cord Med. 1995;18(2):71-74.
8. Mumcuoglu KY. Clinical applications for maggots in wound care. Am J Clin Dermatol. 2001;2(4):219-227.
9. Sherman RA. Maggot versus conservative debridement therapy for the

treatment of pressure ulcers. Wound Repair Regen. 2002;10(4):208-214.
10. Sherman RA. Maggot therapy for treating diabetic foot ulcers unresponsive to conventional therapy. Diabetes Care. 2003 Feb;26(2):446-51.
11. Armstrong DG, Salas P, Short B, et al. Maggot therapy in "lower-extremity hospice" wound care: Fewer amputations and more antibiotic-free days. J Am Podiatr Med Assoc. 2005;95(3):254-257.
12. U.S. Food and Drug Administration (FDA) 510(k). Medical maggots. Summary of Safety and Effectiveness. 510(k) No. K033391. Rockville, MD: FDA. January 12, 2004. Available at http://www.accessdata.fda.gov/cdrh_docs/pdf3/K033391.pdf. Accessed on March 5, 2009.
13. U.S. Food and Drug Administration (FDA) 510(k). Medical maggots. Summary of Safety and Effectiveness. 510(k) No. K072438. Rockville, MD: FDA. October 5, 2007. Available at http://www.fda.gov/cdrh/pdf7/K072438.pdf. Accessed on March 5, 2009.
14. Chan DC, Fong DH, Leung JY, et al. Maggot debridement therapy in chronic wound care. Hong Kong Med J. 2007;13(5):382-386.
15. Gupta A. A review of the use of maggots in wound therapy. Ann Plast Surg. 2008;60(2):224-227.
16. Raynor P, Dumville J, Cullum N. A new clinical trial of the effect of larval therapy. J Tissue Viability. 2004;14(3):104-105.
17. Tantawi TI, Gohar YM, Kotb MM, et al. Clinical and microbiological efficacy of MDT in the treatment of diabetic foot ulcers. J Wound Care. 2007;16(9):379-383.
18. Dumville JC, Worthy G, Bland JM, et al; VenUS II team. Larval therapy for leg ulcers (VenUS II): Randomised controlled trial. BMJ. 2009;338:b773.
19. Soares MO, Iglesias CP, Bland JM, et al; VenUS II team. Cost effectiveness analysis of larval therapy for leg ulcers. BMJ. 2009;338:b825.